

The European Court of Justice Rules on the Patentability of Human Embryonic Stem Cells: No Patents for inventions relying on Human Embryos as Source Material

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The European Court of Justice (ECJ) recently decided in the case C-34/10 on the patentability of human embryonic stem cells (hESCs)¹. The ECJ concludes that totipotent cells are not eligible for patent protection. The ECJ goes even one step further to conclude that any use of a human embryo (except for its own sake) is considered to contravene the *ordre public*. The Decision is binding to all member states of the EU although not for the European Patent Organization and some of its member states which are not also member of the EU. The legal landscape in Europe regarding the question of patentability of hESCs is complex. For example, Germany and Italy both allow manipulating hESC only if they stem from cell lines established prior to a cut-off date (which is 1. January 2002 in Germany; ²). Belgium, Czech Republic, Denmark, Greece, Spain, Finland, France, the Netherlands, Portugal, Sweden and the United Kingdom allow the procurement of hESCs from supernumerary embryos (initially produced for *in vitro* fertilization purposes). Belgium, Spain, Sweden and the United Kingdom even allow the *creation* of human embryos for the procurement of hESCs. The ECJ decision C-34/10 now adds a further piece to the complex legal landscape in Europe. The Court interprets the underlying European Directive 98/44/EG ³ (the Directive) in a very restrictive manner. The Directive, once established to promote the Biotech Industry by creating a common standard for patentability of biotechnological inventions all over Europe, has now become a hindrance for some parts of the industry. The restrictive interpretation of the ECJ will have a very strong influence on the future decisions of national courts in the EU member states and maybe even on the future case law of the EPO.

The Patent

Claims 1, 12, 16 of the contested patent involve a step of cultivating embryonic stem cells (ESCs) to embryoid bodies.

Claim 1 reads:

1. Isolated, purified, progenitor cells with neuronal or glial properties, **obtained from embryonic stem cells**, comprising no more than 15% primitive embryonic and non-neural cells obtainable by the steps of:

a) **cultivation of ES-cells to embryoid bodies**

b) **cultivation of the embryoid bodies into neural precursor cells,**

c) proliferation of the neural precursor cells in growth factor-containing serum-free medium,

d) proliferation of the neural precursor cells from step c) in another growth factor-containing serum-free medium and isolation of the purified neural precursor cells and

¹ Decision of the ECJ of October 18, 2011 (Case C-34/10)

² German Stem Cell Law (StZG), regulating the import and use of hESC (cut-off date 1. Jan. 2002) for use in science

³ Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (OJ 1998 L 213, p. 13)

e) proliferation of the neural precursor cells from step d) in another growth factor-containing serum-free medium and isolation of the purified precursor cells with neuronal or glial properties, or

a') [...] c')

d') proliferation of the neural precursor cells from step c') in another growth factor-containing serum-free medium to spheroids with neuronal or glial differentiation potential and isolation of the neural spheroids

e') proliferation of the neural spheroid from step d') in another growth factor-containing serum-free medium up to the development of a cell layer consisting of glial precursor cells and isolation of the purified precursor cells with glial properties.

Claim 6 specifies that the source of the ESCs may be embryonic germ cells (which are pluripotent, not totipotent), claim 8 specifies that the cells may be of human origin, and further claims are directed to use in therapy of the resulting neuronal progenitor cells. It is important to note that the method for obtaining the hESCs is not part of the claims and the application describes non-destructive ways of obtaining hESCs (paper examples).

The first instance

In the first instance, the German Federal Patent Court in its decision 3 Ni 42/04 ruled that the patent (DE 19756864 to Brüstle) was partially invalid.

The Federal Patent Court reasoned in its decision that at the time of filing, the only way of generating hESC involved the destruction of a human embryo, and therefore, the products and methods claimed necessarily involved the “use of human embryos”. The Federal Patent Court also interpreted the use of the hESC as a “use for industrial or commercial purposes” which is excluded from patentability under §2(2)(1) No.3 PatG.

This provision implements Article 6(2)(c) of the Directive into German Law⁴, and excludes the subject matter from patentability as running counter to the *ordre public*. The exclusion clauses of Art. 2 PatG⁵ (and the corresponding EEC Directive) were interpreted broadly, also in view of §1(1) No.2 of the German Law on the Protection of Human Embryos (EschG)⁶, which – according to the opinion of the court - dominates the rights for obtaining patent protection. The Federal Patent Court thus found that any use involving the “consumption of human embryos” that is not explicitly allowed for reproductive purposes is prohibited and ruled the claims partially invalid.

As far as the invention pertains to embryonic stem cells derived from human embryonic **germ** cells (pluripotent), the patent was maintained as these cells can be provided without “consuming” human embryos.

⁴ The relevant parts of Article 6 of the Directive reads:

1. *Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.*

2. *On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:*

...
(c) *uses of human embryos for industrial or commercial purposes;*

...
⁵ Paragraph 2 of the PatG, as amended for the purposes of implementation of Article 6 of the Directive (BGBl. 2005 I, p. 2521; ‘the PatG’), is worded as follows:

1. *Patents may not be granted for inventions whose commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.*

2. *In particular, patents shall not be awarded for:*

...
(3) *uses of human embryos for industrial or commercial purposes;*

...
The application of points (1) to (3) shall be governed by the appropriate provisions of the [ESchG] (Law on the protection of embryos).’

⁶ Paragraph 1(1), point 2 of the ESchG of 13 December 1990 defines as a criminal offence the artificial fertilisation of ova for a purpose other than inducing pregnancy in the woman from whom the ova originate

The referring decision

In the second instance, the German Federal Court of Justice (BGH), found in its decision Xa ZR 58/07 that the patentability of the claimed methods ultimately depends on the interpretation of Art. 6(2)(c) of the Directive (in particular which activity represents “a use of human embryos for industrial or commercial purposes”). The BGH further noted that the Directive provides no definition for the term ‘embryo’. According to Paragraph 8(1) of the German ESchG, an embryo is a fertilized human ovum capable of development from the time of karyogamy, and any totipotent cell removed from an embryo which is able to divide and develop into an individual under the necessary conditions required. The BGH further found that the subject matter of the claims is not excluded from patentability under § 2(1) PatG if there is at least one way of legally exploiting the invention. “Exploitation” in this context are actions defined in §9 PatG⁷, i.e. (a) the making, offering, putting on the market or using a product which is the subject matter of the patent (b) the use of a process which is the subject matter of the patent and (c) offering, putting on the market, using a product obtained directly by a process which is the subject matter of the patent. Importantly, it was noted that not every exploitation that may be prohibited by law or regulation is automatically against the *ordre public*, for example, a use that is allowed under certain circumstances under the law (in this case the German Law on Stem Cells, StZG) which use falls within the scope of the patent cannot be against the *ordre public* as the legislator implemented this use on behalf of and for the benefit of the people. According to an earlier ECJ Decision, C-377/98 (9.10.2001), the contracting states of the European Union do not have any administrative discretion to interpret EU law such as the exemptions to patentability under Art. 6 of the Directive. This consequently also applies to what is

meant by “uses of human embryos for industrial or commercial purposes”. The Directive does not provide a definition of the term “embryo”: Moreover, whether a use in science is a “use ... for industrial or commercial purposes” is also not derivable from the Biotech Directive as such. Finally the Directive explicitly states that the “exclusion does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it”. In view of the need to find an interpretation for what is meant by “use of human embryos for industrial or commercial purposes” the BGH referred several questions to the ECJ while staying the proceedings before the Court.

Questions referred to the ECJ

The BGH referred the following questions to the ECJ:

1. *What is meant by the term “human embryos“ in Art. 6 (2) (c) of the Directive No. 98/44/EC?*

a) Are all stages of development of human life beginning from the fertilization of the egg cell comprised or must additional requirements be fulfilled as for instance reaching of a certain stage of development?

b) Are the following organisms comprised too:

(1) unfertilized human egg cells in which a nucleus from a mature human cell has been transplanted;

(2) unfertilized human egg cells which have been stimulated to separation and further development by way of parthenogenesis?

c) Are also stem cells comprised which have been derived from human embryos in the blastocyst stage?

2. *What is meant by the term “use of human embryos for industrial or commercial purposes“? Does it*

⁷ §9 PatG corresponds to Art. 28(1) TRIPS

encompass every commercial exploitation in the sense of Art. 6 (1) of the Directive⁸, in particular also a use for the purposes of scientific research?

3. Is a technical teaching excluded from patenting pursuant to Art. 6 (2)(c) of the Directive also in case that the use of the human embryos is not part of the claimed technical teaching of the patent but a necessary requirement for the application of this teaching,

a) because the patent concerns a product whose manufacturing requires the previous destruction of human embryos,

b) or because the patent concerns a method for which such product is needed as starting material?

While the BGH asked the right questions the answers rendered by the ECJ leave a lot of room for speculation and create a good deal of uncertainty in the field of stem cell research, especially with regard to the question of what might constitute an invention susceptible of patent protection in this important field of biomedical research.

Decision of the ECJ

Answers:

The answer to the first question is that:

"- any human ovum after fertilisation, any non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted and any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute a 'human embryo' within the meaning of Article 6(2)(c) of the Directive;

- it is for the referring court to ascertain, in

⁸ Art. 6(1) reads: "1. Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation."

the light of scientific developments, whether a stem cell obtained from a human embryo at the blastocyst stage constitutes a 'human embryo' within the meaning of Article 6(2)(c) of the Directive."

As one may take from the above answer, the ECJ defined a very early development stage in the development of a human body as an "embryonic stage" but the Court did not address the BGHs question as to whether "all stages of development" must be regarded as an embryo. The partly incomplete answer rendered by the ECJ creates substantial uncertainty with regard to which developmental stages of the human body may or may not fall under the term "human embryo". Some repercussions of this incomplete answer on the patentability of inventions making use of early human development stages will be discussed further below.

The answer to the second question is "[...] *that the exclusion from patentability concerning the use of human embryos for industrial or commercial purposes in Article 6(2)(c) of the Directive also covers use for purposes of scientific research, only use for therapeutic or diagnostic purposes which is applied to the human embryo and is useful to it being patentable.*"

The answer to the third question is "[...] *that Article 6(2)(c) of the Directive excludes an invention from patentability where the technical teaching which is the subject-matter of the patent application requires the prior destruction of human embryos or their use as base material, whatever the stage at which that takes place and even if the description of the technical teaching claimed does not refer to the use of human embryos.*"

The very critical statement in this answer is that not only inventions related to stem cells, but rather any invention is excluded from patent protection once the invention uses a human embryo as base material and even if the technology is of no harm to the human embryo. This appears to be a

very broad interpretation of Article 6(2)(c) of the Directive; practical consequences are discussed below.

Reasoning:

Reasoning of the ECJ for the answer to Question 1:

The ECJ interpreted various passages of the Directive, concluding that the legislator intended to exclude any kind of patenting in which the risk exists that the technology might be in conflict with human dignity (Reasons points 32-34). The ECJ concluded from this intention of the legislator that the term 'human embryo' must be construed broadly.

Reasoning of the ECJ for the answer to Question 2:

The ECJ held that a patent generally serves commercial purposes (Reasons point 41-42) and that the Directive itself also recognises this in Recital (14)⁹. The ECJ interpreted the Directive to not distinguish between industrial or commercial purposes and scientific or research purposes. However, the Directive was found to distinguish between industrial/commercial uses on the one hand and therapeutic/diagnostic purposes (to the benefit of the embryo, Recital 42) on the other hand. It was noted that EPO Decision G2/06 came to the same conclusion¹⁰ in this point. Hence, the ECJ came to the conclusion that an invention – even if performed for research purposes only – still serves an industrial/commercial purpose within the meaning of Art. 6 (2)(c) of the Directive.

Reasoning of the ECJ for the answer to Question 3:

⁹ *Recital 14 reads:* "(14) Whereas a patent for invention does not authorise the holder to implement that invention, but merely entitles him to prohibit third parties from exploiting it for industrial and commercial purposes; ..."

¹⁰ Decision of the Enlarged Board of Appeal of 25 November 2008, G 2/06, Official Journal EPO, May 2009, p. 306, paragraphs 25 to 27

The ECJ held that according to the Directive, the list of exclusions¹¹ is not exhaustive and that all processes the use of which runs counter to human dignity are also excluded from patentability. The ECJ further held that it is irrelevant whether the method that requires the "consumption" of human embryos is part of the claims. The ECJ considered irrelevant the question of whether or not the destruction of the embryo may have occurred at a stage long before the implementation of the invention, as in the case of the production of embryonic stem cells from a lineage of stem cells. In the ECJ's view, not excluding such indirect uses would make the provision practically easy to circumvent. Also this point was seen to be in agreement with the EPO decision G2/06¹².

Discussion

The ECJ's interpretation of the Directive as intending to protect human dignity and, hence, its broad interpretation of the term "human embryo" is questionable. It disregards the explicitly stated incentive in the Directive to encourage obtaining elements valuable to medicinal production (Recitals 17 and 18 of the Directive¹³).

¹¹ (a) processes for cloning human beings; (b) processes for modifying the germ line genetic identity of human beings; (c) uses of human embryos for industrial or commercial purposes; (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

¹² G2/06 Reasons point 22

¹³ (17) Whereas significant progress in the treatment of diseases has already been made thanks to the existence of medicinal products derived from elements isolated from the human body and/or otherwise produced, such medicinal products resulting from technical processes aimed at obtaining elements similar in structure to those existing naturally in the human body and whereas, consequently, research aimed at obtaining and isolating such elements valuable to medicinal production should be encouraged by means of the patent system;

(18) Whereas, since the patent system provides insufficient incentive for encouraging research into and production of biotechnological medicines which are needed to combat rare or 'orphan' diseases, the Community and the Member States have a duty to respond adequately to this

Moreover, under the “human dignity” aspect it appears inconsistent to argue that a human embryo cannot serve as source material for an invention and therefore to exclude such inventions from patent protection, while inventions which make use of the “adult” human body, such as e.g. products isolated from the human body, do not give rise to any conflict with the same provision.

What appears to be more of a problem for future patenting practice is that the Decision does not completely define the embryonic stage; it does not define when - in the course of the development of the human body - the embryo stage ends. By ruling that any invention that “requires the prior destruction of human embryos or their use as base material is excluded from patentability, whatever the stage at which such destruction takes place and even if the description of the technical teaching claimed does not refer to the use of human embryos”, opens the door for a very broad interpretation of the exclusion provision under Art. 6(2)(c). The reasoning of the decision does not provide any means of clarifying this ruling. If one takes, as a supplementary means for interpretation the Decision, the opinion of the Advocate General, the only conclusion is that any stage of development of the human body is an “embryo”¹⁴. Seen this way, any technology that would make use of the human body (at any stage of development) as a source material for an invention would be in conflict with the exclusion under Art. 6(2)(c) of the Directive.

The question is therefore: when is “the use of the human body ” as a source material the “use of a human embryo” in the meaning of Art. 6(2)(c). While having defined when the ‘embryo’ begins, the ECJ has failed to define where the

“embryo” ends. For example, whether fetal cells (e.g. from cord blood) can be patented becomes questionable under the ECJ’s ruling; such a technology might be interpreted to be ultimately based on the use of a human embryo as a source material and, hence, to fall under Art.6(2)(c).

Another question that may arise in the future is the question of when a treatment is to the “advantage of an embryo”? For methods involving prenatal diagnosis or also pre-implantation diagnostics (PID), the answer to this question may depend on the diagnostic outcome of the relevant method. How should a patent office or national court decide whether a diagnostic method, which e.g. makes use of cells of an embryo, is excluded by Art.6(2)(c) (because it makes use of an embryo for commercial purposes) or allowed (because the diagnosis benefits the embryo)?

Clearly, while scientific research is not directly impacted by the ECJ’s decision, many projects depend on funding from the pharmaceutical industry. In view of this decision, it is conceivable that many companies may refrain from beginning or continuing efforts in the field of stem cell research. Considering, that the Directive was at one time established to promote the Biotechnology Industry in Europe the present ECJ Decision appears to fail in its full support of this initial goal.

problem;

¹⁴ From the conclusions of the Advocate General: “The concept of a human embryo applies from the fertilization stage to the initial totipotent cells and to the entire ensuing process of the development and formation of the human body. That includes the blastocyst.”